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TECH CENTER 1600/2000
Patent

Attorney's Docket No. 003300-914

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)	
)	
KJELL OLMARKER)	Group Art Unit: 1614
)	
Application No.: 10/092,919)	Examiner: Unassigned
)	
Filed: March 8, 2002)	Confirmation No.: 1488
)	
For: NOVEL USE OF CYTOKINE)	
INHIBITORS)	

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. §1.56, Applicant provides information in conformance with 37 C.F.R. §§1.97 and 1.98.

Applicant provides a copy of an International-Type Search Report that was issued in conjunction with counterpart Swedish Application No. 0200667-4 dated November 15, 2002. Copies of each of the seven (7) items cited in the Search Report are additionally provided.


Applicant provides a copy of the International Search Report that issued in conjunction with counterpart International Application No. PCT/SE03/00347 on June 23, 2003. Copies of each of the five (5) items cited in the International Search Report are additionally provided.

For the convenience of the Examiner, a form PTO-1449 is attached where the twelve (12) items are listed. It is requested that an Examiner-initialed copy of this form be returned to the undersigned once the above items are considered.

The examination and allowance of the Application are respectfully requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 
Benton S. Duffett, Jr.
Registration No. 22,030

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Filed: August 26, 2003

AUG 26 2003

SHEET 1 OF 1

Substitute for forms 1001A/PTO & 1449B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

ATTORNEY'S DKT No.
003300-914

APPLICATION No.
10/092,919

APPLICANT
KJELL OLMARKER

FILING DATE
March 8, 2002

GROUP
1614

U.S. PATENT DOCUMENTS

Examiner Initials	Document Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Issue/Publication Date (MM-DD-YYYY)
	5,196,430		MANDRELL <i>et al.</i>	March 23, 1993
	5,994,376		FREYNE <i>et al.</i>	November 30, 1999
	6,348,602		FOWLER <i>et al.</i>	February 19, 2002

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AUG 27 2003

TECH CENTER 1600/2900

FOREIGN PATENT DOCUMENTS

Examiner Initials	Document Number	Kind Code (if known)	Country	Date of Publication (MM-DD-YYYY)	Translation Yes	No
	WO 89/05145		International	June 15, 1989		
	WO 98/06715		International	February 19, 1998		
	WO 01/57018		International	August 9, 2001		
	WO 01/58469		International	August 16, 2001		

NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	STN International, File ZCAPLUS, Accession No. 2002:199887, Document No. 136:323691, Kaser, Arthur <i>et al.</i> , "Infliximab in Severe Steroid-Refractory Ulcerative Colitis: A Pilot Study", & Wiener Klinische Wochenschrift (2001), 113(23-24), 930-933.
	STN International, File MEDLINE, Accession No. 2000046083, Document No. 20046083, Heller T. <i>et al.</i> , "Treatment of Severe Esophageal Crohn's Disease With Infliximab", & INFLAMMATORY BOWEL DISEASES, (1999 Nov.) 5 (4) 279-82.
	STN International, File MEDLINE, Accession No. 2001011857, Document No. 20409486, Jovic N., "[Pharmacotherapy of Inflammatory Bowel Disease]. "Farmakoterapija Inflammatory Bolesti Creva", & ACTA CHIRURGICA JUGOSLAVICA, (2000) 47 (1-2) 51-5.
	STN International, FILE MEDLINE, Accession No. 2001419273, Document No. 21360250, Blam M.E., "Integrating Anti-Tumor Necrosis Factor Therapy in Inflammatory Bowel Disease: Current and Future Perspectives", AMERICAN JOURNAL OF GASTROENTEROLOGY, (2001 Jul.) 96 (7) 1977-97.
	STN International, File MEDLINE, Accession No. 2001553668, Document No. 21486185, Travis S.P. <i>et al.</i> , "Treatment of Intestinal Behcet's Syndrome With Chimeric Tumour Necrosis Factor Alpha Antibody", & GUT, (2001 Nov.) 49 (5) 725-8.

Examiner
Signature

Date
Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with M.P.E.P. § 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL-TYPE SEARCH REPORT

(PCT Article 15.5)

National application No. 0200667-4	Country or Office of filing SE	Applicant's or agent's file reference SE-2026010
Filing date (<i>day/month/year</i>) 5 March 2002	(Earliest) Priority Date (<i>day/month/year</i>)	
Applicant A+ SCIENCE INVEST AB		

Date of request for international-type search 5 March 2002	International-type search request No. SE 02/00179
---	--

This international-type search report has been prepared by this International Searching Authority and is transmitted to the applicant.

This international-type search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (See Box I).

2. ☐ Unity of invention is lacking (See Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international-type search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ transcribed by this Authority.

INTERNATIONAL-TYPE SEARCH REPORT

Search request No.
ITS/SE02/00179

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international-type search report has not been established in respect of certain claims for the following reasons:

1. ☒ Claims No.: 26-50
because they relate to subject matter not required to be searched by this Authority, namely:
**A method for treatment of the human or animal body by therapy,
see rule 39.1**
2. ☐ Claims No.:
because they relate to parts of the national application that do not comply with the prescribed requirements
to such an extent that no meaningful international-type search can be carried out, specifically:

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international-type search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international-type search report covers only those claims for which fees were paid, specifically claims No.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international-type search report is restricted to the invention first mentioned in the claims, it is covered by claims No.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL-TYPE SEARCH REPORT

Search request No.

SE 02/00179

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 8905145 A1 (HOECHST-ROUSSEL PHARMACEUTICALS INCORPORATED), 15 June 1989 (15.06.89), pages 11-12 and claims --	1-25
X	US 5196430 A (GERALD L. MANDRELL ET AL), 23 March 1993 (23.03.93), column 10 and claims --	1-25
X	US 6348602 B1 (KERRY W. FOWLER ET AL), 19 February 2002 (19.02.02), see especially claim 21 --	1-25

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international-type search

12 November 2002

Date of mailing of the international-type search report

2002-11-15

Name and mailing address of the ISA/

Swedish Patent Office

Box 5055, S-102 42 STOCKHOLM

Facsimile No. +46 8 666 02 86

Authorized officer

Göran Karlsson/EÖ

Telephone No. +46 8 782 25 00

INTERNATIONAL-TYPE SEARCH REPORT

Search request No.

SE 02/00179

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5994376 A (EDDY JEAN EDGARD FREYNE ET AL), 30 November 1999 (30.11.99), columns 26-27 and claims --	1-25
X	WO 0157018 A1 (ABBOTT LABORATORIES), 9 August 2001 (09.08.01), page 1 and claims --	1-25
X	WO 9806715 A1 (SMITHKLINE BEECHAM CORPORATION), 19 February 1998 (19.02.98), pages 17-18 and claim 12 --	1-25
X	WO 0158469 A1 (WAX, MARTIN, B.), 16 August 2001 (16.08.01), pages 4-5 and claim 14 -- -----	1-25

INTERNATIONAL-TYPE SEARCH REPORT

Information on patent family members

28/10/02

Search request No.

SE 02/00179

WO	8905145	A1	15/06/89	AT	118347	T	15/03/95
				AU	632466	B	07/01/93
				AU	652094	B	11/08/94
				AU	2828589	A	05/07/89
				AU	3564193	A	03/06/93
				CA	1334508	A	21/02/95
				DE	3853067	D,T	14/06/95
				DK	391989	A	10/08/89
				EP	0344288	A,B	06/12/89
				SE	0344288	T3	
				IE	69868	B,L	16/10/96
				IE	883687	L	11/06/89
				IL	88656	A	08/07/93
				IL	102919	A	26/08/94
				IL	102920	A	30/05/94
				IL	102921	A	30/05/94
				IL	102922	A	30/05/94
				JP	2502542	T	16/08/90
				JP	2507105	B	12/06/96
				KR	9608235	B	21/06/96
				US	4965271	A	23/10/90
				US	5196429	A	23/03/93
				US	5196430	A	23/03/93
				US	5272153	A	21/12/93
				ZA	8809235	A	26/09/90

INTERNATIONAL-TYPE SEARCH REPORT

Information on patent family members

28/10/02

Search request No.

SE 02/00179

US	5196430	A	23/03/93	AT	118347	T	15/03/95
				AU	632466	B	07/01/93
				AU	652094	B	11/08/94
				AU	2828589	A	05/07/89
				AU	3564193	A	03/06/93
				CA	1334508	A	21/02/95
				DE	3853067	D,T	14/06/95
				DK	391989	A	10/08/89
				EP	0344288	A,B	06/12/89
				SE	0344288	T3	
				IE	69868	B,L	16/10/96
				IE	883687	L	11/06/89
				IL	88656	A	08/07/93
				IL	102919	A	26/08/94
				IL	102920	A	30/05/94
				IL	102921	A	30/05/94
				IL	102922	A	30/05/94
				JP	2502542	T	16/08/90
				JP	2507105	B	12/06/96
				KR	9608235	B	21/06/96
				US	4965271	A	23/10/90
				US	5196429	A	23/03/93
				US	5272153	A	21/12/93
				WO	8905145	A	15/06/89
				ZA	8809235	A	26/09/90
				US	5096906	A	17/03/92
				AT	151290	T	15/04/97
				AU	619732	B	06/02/92
				AU	637542	B	27/05/93
				AU	668982	B	23/05/96
				AU	1150588	A	27/07/88
				AU	1291892	A	14/05/92
				AU	4602793	A	18/11/93
				CA	1313137	A	26/01/93
				DE	3752048	D,T	02/10/97
				DK	482088	A	28/10/88
				EP	0279079	A,B	24/08/88
				SE	0279079	T3	
				ES	2103255	T	16/09/97
				GR	3024054	T	31/10/97
				IE	355487	L	30/06/88
				IE	873554	L	30/06/88
				IL	84934	A	26/08/94
				IL	100533	A	30/05/94
				IL	100535	A	30/05/94
				IL	100536	A	30/05/94
				IL	106854	A	14/05/96
				IL	106858	D	00/00/00
				IL	106859	A	16/10/96
				IL	106861	A	18/02/97
				JP	2507012	B	12/06/96
				KR	9615726	B	20/11/96
				WO	8804928	A	14/07/88
				ZA	8709754	A	26/07/89

INTERNATIONAL-TYPE SEARCH REPORT

Information on patent family members

28/10/02

Search request No.

SE 02/00179

US	6348602	B1	19/02/02	US	2002065302	A	30/05/02
				AU	4137001	A	03/07/01
				EP	1242371	A	25/09/02
				WO	0146136	A	28/06/01

US	5994376	A	30/11/99	AT	214052	T	15/03/02
				AU	702947	B	11/03/99
				AU	5275596	A	23/10/96
				DE	69619661	D	00/00/00
				DK	819122	T	01/07/02
				EP	0819122	A,B	21/01/98
				SE	0819122	T3	
				HK	1007880	A	00/00/00
				JP	11503136	T	23/03/99
				NO	974602	A	06/10/97
				NZ	304877	A	29/06/99
				SI	819122	T	00/00/00
				US	6403805	B	11/06/02
				US	2002068830	A	06/06/02
				CA	2216653	A	10/10/96
				CN	1068591	B	18/07/01
				CN	1181072	A	06/05/98
				CZ	9703149	A	16/12/98
				HR	960155	A	31/10/97
				HU	9801575	A	28/01/99
				IL	117807	A	14/06/01
				PL	322654	A	16/02/98
				WO	9631485	A	10/10/96
				ZA	9602754	A	06/10/97

WO	0157018	A1	09/08/01	NONE			

WO	9806715	A1	19/02/98	EP	0922042	A	16/06/99
				JP	2001506230	T	15/05/01

WO	0158469	A1	16/08/01	AU	3793901	A	20/08/01

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 21002524	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/SE 03/00347	International filing date (day/month/year) 4 March 2003	(Earliest) Priority Date (day/month/year) 5 March 2002
Applicant PHARMASURGICS AB ET AL		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE03/00347

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 25-48
because they relate to subject matter not required to be searched by this Authority, namely:
A method for treatment of the human or animal body by therapy,
see rule 39.1
2. ☒ Claims Nos.: 1-24
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see next sheet
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Present claims 1-24 relate to a substance defined by reference to a desirable characteristic or property, namely that inhibits a pro-inflammatory cytokine for treatment of a wound by improving wound healing. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and / or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lacks clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Further, the wording "a substance that inhibits a pro-inflammatory cytokine" and similar expressions in the claims are not clear and concise. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has mainly been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely the use of the example compound infliximab for the production of a pharmaceutical composition for treatment of a wound by improving wound healing.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established will not be the subject of an international preliminary examination (Rule 66.1 (e) PCT). This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/00347

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File ZCAPLUS, accession no. 2002:199887, document no. 136:323691, Kaser, Arthur et al, "Infliximab in severe steroid-refractory ulcerative colitis: A pilot study", & Wiener Klinische Wochenschrift (2001), 113(23-24), 930-933 --	1-24
X	STN International, File MEDLINE, accession no. 2000046083, document no. 20046083, Heller T. et al, "Treatment of severe esophageal Crohn's disease with infliximab", & INFLAMMATORY BOWEL DISEASES, (1999 Nov) 5 (4) 279-82 --	1-24

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

18 June 2003

Date of mailing of the international search report

23-06-2003

Name and mailing address of the ISA/

Swedish Patent Office

Box 5055, S-102 42 STOCKHOLM

Facsimile No. +46 8 666 02 86

Authorized officer

GÖRAN KARLSSON/BS

Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/00347

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STN International, File MEDLINE, accession no. 2001011857, document no. 20409486, Jojic N., "[Pharmacotherapy of inflammatory bowel disease]. "Farmakoterapija inflamatornih bolesti creva", & ACTA CHIRURGICA JUGOSLAVICA, (2000) 47 (1-2) 51-5 --	1-24
X	STN International, File MEDLINE, accession no. 2001419273, document no. 21360250, Blam M.E., "Integrating anti-tumor necrosis factor therapy in inflammatory bowel disease: current and future perspectives", AMERICAN JOURNAL OF GASTROENTEROLOGY, (2001 Jul) 96 (7) 1977-97 --	1-24
X	STN International, File MEDLINE, accession no. 2001553668, document no. 21486185, Travis S.P. et al, "Treatment of intestinal Behcet's syndrome with chimeric tumour necrosis factor alpha antibody", & GUT, (2001 Nov) 49 (5) 725-8 -----	1-24

1

AN 2002:199887 ZCAPLUS
DN 136:323691
TI Infliximab in severe steroid-refractory ulcerative colitis: A pilot study
AU Kaser, Arthur; Mairinger, Thomas; Vogel, Wolfgang; Tilg, Herbert
CS Division of Gastroenterology and Hepatology, Department of Medicine,
University Hospital Innsbruck, Austria
SO Wiener Klinische Wochenschrift (2001), 113(23-24), 930-933
CODEN: WKWOAO; ISSN: 0043-5325
PB Springer-Verlag Wien
DT Journal
LA English
CC 15-3 (Immunochemistry)
Section cross-reference(s): 1
ST infliximab TNF alpha ulcerative colitis
IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alpha; infliximab for treatment of severe steroid-refractory
ulcerative colitis)
IT Drug resistance
Human
Wound healing
(infliximab for treatment of severe steroid-refractory ulcerative
colitis)
IT Intestine, disease
(ulcerative colitis; infliximab for treatment of severe
steroid-refractory ulcerative colitis)
IT 170277-31-3, Infliximab
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(infliximab for treatment of severe steroid-refractory ulcerative
colitis)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2000046083 MEDLINE
 DN 20046083 PubMed ID: 10579121
 TI Treatment of severe esophageal Crohn's disease with **infliximab**.
 AU Heller T; James S P; Drachenberg C; Hernandez C; Darwin P E
 CS Department of Medicine, University of Maryland School of Medicine,
 Baltimore 21201, USA.
 SO INFLAMMATORY BOWEL DISEASES, (1999 Nov) 5 (4) 279-82.
 Journal code: 9508162. ISSN: 1078-0998.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199912
 ED Entered STN: 20000113
 Last Updated on STN: 20030225
 Entered Medline: 19991221
 AB Esophageal **ulceration** with fistula is an uncommon manifestation
 of Crohn's disease. Typical presentation of symptomatic esophageal
 Crohn's disease may include dysphagia, odynophagia, weight loss, and chest
 discomfort. We present a patient with severe esophageal and skin
 involvement of Crohn's disease that was progressive despite conventional
 therapy including prednisone and 6-mercaptopurine. The diagnosis of
 Crohn's was based on the presence of typical clinical, endoscopic, and
 pathologic findings, including granulomas in the skin **ulcer** and
 the absence of infectious etiologies. The patient had a nearly complete
 resolution of her esophageal disease with a single infusion of
infliximab.
 CT Check Tags: Case Report; Female; Human
 Aged
 *Antibodies, Monoclonal: AD, administration & dosage
 Crohn Disease: CO, complications
 Crohn Disease: DI, diagnosis
 *Crohn Disease: DT, drug therapy
 *Esophageal Diseases: DT, drug therapy
 Esophageal Diseases: ET, etiology
 Esophageal Diseases: PA, pathology
 *Esophageal Fistula: DT, drug therapy
 Esophageal Fistula: ET, etiology
 Esophageal Fistula: PA, pathology
 Esophagoscopy
 Follow-Up Studies
 Infusions, Intravenous
 Severity of Illness Index
 Treatment Outcome
 CN 0 (Antibodies, Monoclonal); 0 (**infliximab**)

AN 2001011857 MEDLINE
DN 20409486 PubMed ID: 10953366
TI [Pharmacotherapy of inflammatory bowel disease].
Farmakoterapija inflamatornih bolesti creva.
AU Jojic N
CS KBC Zvezdara, Centar za gastroenterologiju, Metabolicko odeljenje,
Beograd.
SO ACTA CHIRURGICA IUGOSLAVICA, (2000) 47 (1-2) 51-5. Ref: 22
Journal code: 0372631. ISSN: 0354-950x.
CY Yugoslavia
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Serbo-Croatian
FS Priority Journals
EM 200010
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001026
AB Inflammatory bowel disease (IBD) encompasses **ulcerative** colitis
and Crohn's disease. Since the etiology of both diseases, is undetermined
the causal therapy do not exist. Medical treatment has focused on
nonspecific suppressions of the inflammatory process. There are four
groups of IBD drugs: anti-inflammatory medicaments, immunomodulators,
antidiarrheal agents, and biologic therapy. In a last year
immunosuppressives become the very essential IBD drugs. Azathioprine is
drug of choice for chronically active Crohn's disease; methotrexate become
the second line immunosuppressive drug. It appears that anti-TNG
monoclonal antibodies, cA2 (**infliximab**) may produce rapid
control of active Crohn's disease and achieve tissue healing. Topically
acting glucocorticosteroids are a safer than standard glicocorticosteroids
in ileocolonic Crohn's disease. Cyclosporin is becoming a drug of choice
in severely active **ulcerative** colitis. Anti-inflammatory
agents, sulfasalazine and 5-ASA drugs are recommended in treatment mild
and moderately active IBD and as maintenance treatment in
ulcerative colitis. Corticosteroids still have the main role in
the treatment of active IBD. There is no convincing data for efficacy of
corticosteroids as maintenance therapy.
CT Check Tags: Human
English Abstract
*Inflammatory Bowel Diseases: DT, drug therapy

AN 2001419273 MEDLINE
 DN 21360250 PubMed ID: 11467623
 TI Integrating anti-tumor necrosis factor therapy in inflammatory bowel disease: current and future perspectives.
 AU Blam M E; Stein R B; Lichtenstein G R
 CS Department of Medicine, Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, Philadelphia 19104-4283, USA.
 SO AMERICAN JOURNAL OF GASTROENTEROLOGY, (2001 Jul) 96 (7) 1977-97. Ref: 103
 Journal code: 0421030. ISSN: 0002-9270.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW LITERATURE)
 LA English
 FS Priority Journals
 EM 200108
 ED Entered STN: 20010903
 Last Updated on STN: 20030225
 Entered Medline: 20010830
 AB Crohn's disease and **ulcerative** colitis are two idiopathic inflammatory disorders of the GI tract. Manifestations of disease can be severe and lead to long term therapy with a variety of medications and/or surgery. Standard medical therapy consists of agents that either treat suppurative complications or modulate the inflammatory cascade in a nonspecific manner. Many specific chemokine and cytokine effectors that promote intestinal inflammation have been identified. Such work has led to experimental clinical trials with a variety of cytokine antagonists. Compounds directed against one such cytokine, tumor necrosis factor alpha (TNF), have demonstrated the greatest clinical efficacy to date. This is consistent with scientific observations that suggest a central role for TNF in the inflammatory cascade. **Infliximab** is a chimeric monoclonal antibody against TNF that has been demonstrated to be effective for the treatment of Crohn's disease. **Infliximab** is Food and Drug Administration approved for the treatment of Crohn's disease. There exist several other TNF antagonists in various phases of investigation, including the monoclonal antibody CDP 571, the fusion peptide etanercept, the phosphodiesterase inhibitor oxpentifylline, and thalidomide. The clinical efficacy of these agents and the role of TNF in the pathogenesis of inflammatory bowel disease is reviewed.
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
 Antibodies, Monoclonal: TU, therapeutic use
 Clinical Trials
 Forecasting
 Gastrointestinal Agents: TU, therapeutic use
 Immunoglobulin G: TU, therapeutic use
 Inflammatory Bowel Diseases: DT, drug therapy
 Inflammatory Bowel Diseases: IM, immunology
 *Inflammatory Bowel Diseases: TH, therapy
 Models, Biological
 Pentoxifylline: TU, therapeutic use
 Receptors, Tumor Necrosis Factor: TU, therapeutic use
 Thalidomide: TU, therapeutic use
 *Tumor Necrosis Factor: AI, antagonists & inhibitors
 RN 185243-69-0 (TNFR-Fc fusion protein); 50-35-1 (Thalidomide); 6493-05-6 (Pentoxifylline)
 CN 0 (Antibodies, Monoclonal); 0 (CDP 571); 0 (Gastrointestinal Agents); 0 (Immunoglobulin G); 0 (Receptors, Tumor Necrosis Factor); 0 (Tumor Necrosis Factor); 0 (**infliximab**)

AN 2001553668 MEDLINE
 DN 21486185 PubMed ID: 11600479
 TI Treatment of intestinal Behcet's syndrome with chimeric tumour necrosis factor alpha antibody.
 AU Travis S P; Czajkowski M; McGovern D P; Watson R G; Bell A L
 CS Gastroenterology Unit, Derriford Hospital, Plymouth PL6 8DH, UK..
 simon.travis@orh.nhs.uk
 SO GUT, (2001 Nov) 49 (5) 725-8.
 Journal code: 2985108R. ISSN: 0017-5749.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 200112
 ED Entered STN: 20011016
 Last Updated on STN: 20030225
 Entered Medline: 20011205
 AB Few patients with Behcet's syndrome have gastrointestinal ulceration. Such patients are difficult to treat and have a higher mortality. Faced with refractory symptoms in two patients with intestinal Behcet's, we used the tumour necrosis factor alpha (TNF-alpha) monoclonal antibody **infliximab** to induce remission. Both women (one aged 27 years, the other 30 years) presented with orogenital ulceration, pustular rash, abdominal pain, bloody diarrhoea due to colonic ulceration, weight loss, and synovitis. One had thrombophlebitis, digital vasculitis, perianal fistula, and paracolic abscess; the other had conjunctivitis and an ulcer in the natal cleft. Treatment with prednisolone, methyl prednisolone, and thalidomide in one and prednisolone, colchicine, and cyclosporin in the other was ineffective. After full discussion, **infliximab** (3 mg/kg, dose reduced because of recent sepsis in one, and 5 mg/kg in the other) was administered. Within 10 days the ulcers healed, with resolution of bloody diarrhoea and all extraintestinal manifestations. A second infusion of **infliximab** was necessary eight weeks later in one case, followed by sustained (>15 months) remission on low dose thalidomide. Remission was initially sustained for 12 months in the other but thalidomide had to be stopped due to intolerance, and a good response to retreatment lasted only 12 weeks without immunosuppression, before a third infusion. The cause of Behcet's syndrome is unknown but peripheral blood CD45 gammadelta T cells in Behcet's produce >50-fold more TNF-alpha than controls when stimulated with phorbol myristate acetate and anti-CD3. **Infliximab** could have a role for inducing remission in Behcet's syndrome.
 CT Check Tags: Case Report; Female; Human
 Adult
 Anti-Inflammatory Agents, Steroidal: TU, therapeutic use
 *Antibodies, Monoclonal: TU, therapeutic use
 *Behcet Syndrome: DT, drug therapy
 Drug Therapy, Combination
 *Gastrointestinal Agents: TU, therapeutic use
 Immunosuppressive Agents: TU, therapeutic use
 *Intestinal Diseases: DT, drug therapy
 Remission Induction
 Thalidomide: TU, therapeutic use
 Treatment Outcome
 RN 50-35-1 (Thalidomide)
 CN 0 (Anti-Inflammatory Agents, Steroidal); 0 (Antibodies, Monoclonal); 0 (Gastrointestinal Agents); 0 (Immunosuppressive Agents); 0 (**infliximab**)